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ON THE REACTIONS OF THIOURAZOLES AND THIOURAZOLE SALTS.

I. A STUDY OF THE REACTION BETWEEN SODIUM 1-PHENYL-3-THIOURAZOLE AND ETHYL IODIDE.

II. A STUDY OF 1,4-DIPHENYL-5-THIOURAZOLE.

DISSERTATION.

Submitted to the board of University Studies of
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Degree of Doctor of
Philosophy.

BY
Joseph Chandler
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Acknowledgment should also be made of the valuable assistance of Dr. H.C.Robertson, Jr., by whom the conductivity measurements were made.

I. A STUDY OF THE REACTION BETWEEN SODIUM 1-PHENYL-3-THIOURAZOLE AND ETHYL IODIDE.

For several years there has been in progress in this laboratory an extended investigation of the mechanism of the reaction between alkyl halides and various substances, such as ethylates, phenolates and urazole salts. This problem has been attacked by reaction velocity methods with very satisfactory results. The infomation sought has been somewhat extended, including the relative reaction velocities of various alkyl halides and the exact mechanism by which the reactions take place. We have subjected the various theories previously proposed to experimental investigation and have undertaken finally a thorough study of the question whether the ethylate, phenolate, urazole salt, etc. reacts with the alkyl halide simply in the ionic state or whether both ions and molecules react side by side. The present investigation deals chiefly with this last question. The substances used were sodium 1-phenyl-3-thiourazole and ethyl iodide. The reaction was studied in absolute alcohol at 25° in concentrations varying from N/4 to N/64. The results obtained seem to establish very firmly the fact that in reactions of this type both the ionic and the molecular forms of the salts react side by side with the alkyl halide, each with its own characteristic velocity.

The study of the reaction between 1-phenyl-3-thiourazole and ethyl iodide was begun by Brunel and Acree[1] in 1905 in 50 per cent alcoholic solution at 25°. This work, however, was only preliminary and no conclusions were reached.

In 1906 the problem was taken up by Shadinger and Acree[2] on a more extended scale. Their object was two-fold; first, to determine as far as possible the exact mechanism of the reaction, and, second, to ascertain the relative reaction velocities of the various alkyl halides by varying both the alkyl group and the halide. This work was carried out in 50 per cent alcoholic solution at both 25° and 50°. They reviewed the various theories previously proposed for the mechanism of such reactions: (1) the dissociation theory of Bruyn and Steger, (2) the bivalent carbon theory of Nef, and (3) the complex cation theory of Euler. Their results were not in agreement with any of these theories. They came to the conclusion that the ethyl iodide molecule reacts with the urazole anion possibly with the formation of an intermediate unstable anion of the type $C_2H_5I \cdot \bar{O}H$. They did not investigate directly the question whether both ions and molecules react. Their second problem, the investigation of the relative reaction velocities of various alkyl halides, was taken up thoroughly. Their work included methyl, ethyl, *n*-propyl, *n*-butyl, *n*-hexyl, *n*-octyl, *n*-cetyl,

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[1] Am. Chem. Journ., 43, 550
[2] Ibid, 39, 226.

iso-amyl, iso-propyl, iso-butyl, tertiary butyl and allyl iodides, ethyl, *n*-propyl, *n*-butyl, iso-amyl, iso-propyl, iso-butyl, and tertiary butyl bromides, and *n*-propyl, *n*-butyl, iso-amyl, iso-propyl, iso-butyl, and tertiary butyl chlorides. The velocity constant was found to vary widely with the different halides, a difference in constitution also giving a difference in reaction velocity. In general the secondary alkyl halide was found to be less reactive than the primary, and the tertiary still less than the secondary.

The question whether sodium 1-phenyl-3-thiourazole reacts in both ionic and molecular form was first taken up systematically by Nirdlinger, Rogers and Acree.[1] Their work was carried out in absolute alcohol at 25° by using sodium 1-phenyl-3-thiourazole and ethyl iodide; these substances were also used in the present work in different concentrations and under slightly different conditions. They used concentrations varying from 0.3 N to 0.025 N.

The course of the reaction was followed by titrating the reaction mixture at the end of any time period T with a standard solution of iodine and thus measuring the amount of unchanged sodium 1-phenyl-3-thiourazole present. The concentration of the substance at the beginning of reaction was also determined by titration with the same iodine solutions. The data thus secured were substituted in the general equation for obtaining the velocity constant of a bimolecular reaction when the reacting quantities are equimolecular,

[1] This work will soon be published.

$K_V = AK = \frac{1}{T} \quad \frac{x}{A - x}$, in which

K_V is the velocity constant for the reaction,

x is the amount changed at the time T, and

A-x is the amount unchanged at the time T.

The value obtained for K_V was multiplied by V, the volume of the solution containing a gram molecule of the salt, in order to reduce the velocity constant to that of a normal solution of ionization α. This procedure gives the equation,

$$K_n = V \times K_V.$$

A general equation had previously been deduced by Acree and his co-workers on the assumption that both ions and molecule react:

$$\frac{dx}{dt} = K_i \alpha \ (A-x) \ (B-x) + K_m(1-\alpha) \ (A-x) \ (B-x)$$

$$= \left[K_i \alpha + K_m \ (1-\alpha)\right] (A-x) \ (B-x)$$

On integration and collection of the constants this reduces to the equation

$$K_V \times V = K_n = K_i \alpha + K_m \ (1-\alpha), \text{ in which}$$

K_n is the velocity constant for the reaction in normal concentration of ionization α,

K_i is the velocity constant of the 1-phenyl-3-thiourazole anions,

K_m is the velocity constant of the sodium 1-phenyl-3-thiourazole molecules,

α is the per cent of ionization of the sodium 1-phenyl-3-thiourazole in the concentration used, and

$(1-\alpha)$ is the concentration of the sodium 1-phenyl-3-thiourazole molecules.

The values of $\mathcal{L}$ and $1-\mathcal{L}$ were obtained by conductivity measurements. The values for K_n, $\mathcal{L}$ and $(1-\mathcal{L})$ obtained, as stated above, were substituted in this equation and the resulting equations solved simultaneously for K_i and K_m. The values secured were fairly constant, mean values $K_i = 0.435$ and $K_m = 0.17$ being obtained. This gives a ratio $\frac{K_i}{K_m} = 2.5$. In other words, the 1-phenyl-3-thiourazole anions react 2.5 times as rapidly as the sodium 1-phenyl-3-thiourazole molecules. From the results obtained Nirdlinger and Rogers reached the conclusion that in this reaction the reaction velocity is a function of the concentrations of both the urazole ions and the nonionized urazole salt.

The present investigation is a more accurate confirmation of the work of Nirdlinger and Rogers by the use of the same substances, sodium 1-phenyl-3-thiourazole and ethyl iodide.. The work was carried out at 25° in absolute alcohol, the concentrations being N/4, N/8, N/16, N/32 and N/64. The method of procedure is fully discussed in the experimental part. In the N/4, N/8, and N/16 solutions equimolecular quantities of urazole salt and alkyl halide were used, and the velocity constant was obtained by substituting the proper data in the equation

$$K_V = \frac{1}{T} \quad \frac{x}{A-x}.$$

In the very dilute solutions, N/32 and N/64, however, N/8 ethyl iodide was used and the figures obtained were subs-

tituted in the more general equation

$$K_V = \frac{A}{(B-A)0.4343} \; \frac{1}{T} \; \log \frac{A(B-x)}{B(A-x)},\ ,$$

in which A represents the initial concentration of urazole salt and B the initial concentration of alkyl halide. The excess of alkyl halide was used for the twofold purpose of increasing the speed of the reaction and of miminizing the error due to loss of the volatile alkyl halide by evaporation during the preparation of the solutions. The individual values of K_V in each series showed good agreement and the means of duplicate series checked each other, in general, within 1 per cent. The agreement of values for K_n was, of course, the same. The value for K_n increases gradually from N/4 to N/64 solutions, as would be expected from the results of Nirdlinger and Rogers.

Conductivity measurements of solutions of sodium 1-phenyl-3-thiourazole having the concentrations used in this work were made by Dr. H. C. Robertson, Jr. From these values, $\mathcal{L}$, the ionic concentration, and $(1-\mathcal{L})$, the molecular concentration, were calculated.

The values obtained for K_n, $\mathcal{L}$, and $(1-\mathcal{L})$ were substituted in the equations

$$K_{n\,1} = K_i\,\mathcal{L}_1 + K_m(1-\mathcal{L}_1),$$
$$K_{n\,2} = K_i\,\mathcal{L}_2 + K_m(1-\mathcal{L}_2), \text{ etc.,}$$

and the resulting equations solved simultaneously for K_i and K_m. Each equation was compared with every other to obtain as many individual values as possible. The values obtained for K_i vary from 0.427 to .455 and those for

K_m from 0.125 to 0.135. The mean values obtained were:-

$K_i = 0.447$ $K_m = 0.131$ This gives the ratio $\frac{K_i}{K_m} = 3.43$, that is the anions of sodium 1-phenyl-3-thiourazole react 3.43 times as rapidly with ethyl iodide as do the molecules. Nirdlinger and Rogers obtained the values $K_i = 0.435$, $K_m = 0.17$, and $\frac{K_i}{K_m} = 2.5$. It is seen that these values agree fairly closely with those obtained in the present investigation. The discrepancy is probably due to the different method of preparing solutions of sodium 1-phenyl-3-thiourazole. In making up solutions they used crystallized sodium 1-phenyl-3-thiourazole which contains two molecules, or 20.07 per cent, of water of crystallization. In the present work, as is described more fully in the experimental part, the sodium salt was obtained by treating weighed quantities of 1-phenyl-3-thiourazole with the calculated quantity of carefully standardized sodium ethylate in absolute alcohol. Practically anhydrous solutions were then obtained while those of Nirdlinger and Rogers contained considerable quantities of water, especially in the more concentrated solutions. Whether this difference in the values obtained is due wholly to the presence of water will be investigated in the near future.

The question of the relative reaction of ions and molecules has furthermore been investigated by using sodium phenolate and sodium ethylate with methyl and ethyl iodide, ethyl bromide and benz- and acet-imido esters. The results obtained agree closely with those derived

from this investigation. Good constants for K_i and K_m have been obtained in all cases. In some transformations the ion reacts many times as rapidly as the molecule, whereas in the chemical changes of imidoesters the reaction velocities of the ethylate ions and molecules are nearly equal. The value of the constants obtained for the various substances are given in Table

In conclusion it can be stated that all the results obtained up to the present are entirely in harmony with the theory that in reactions of the type under investigation both ions and molecules react side by side, each with their own characteristic velocity.

EXPERIMENTAL.

Burettes.

The burettes used in this work were made by Greiner with an accuracy corresponding to the Bureau of Standards specifications. In order to avoid the error of parallax the graduation at each cubic centimeter was continued completely around the burette and the other divisions were made over half the distance around. The tip was made especially long and slender with a very fine opening. The burette used for the titration with iodine was calibrated with especial care. The accuracy of graduation was carefully determined by measurement with a cathetometer and found to be quite uniform. The scale was illuminated by a small electric lamp during the measurement. In this manner an accuracy of 0.01 mm., or 0.001 c.c., was ordinarily reached. The burette was then carefully calibrated by weighing the quantity delivered by successive 5 c.c. portions. The cathetometer was used in making these readings. In all cases five minutes was allowed for drainage. In the calibration an accuracy of two or three thousandths of a cubic centimeter was ordinarily obtained in duplicate readings. In the calibrations the electric light was again used to illuminate the scale and meniscus. The average total capacity of this burette was 50.01 c.c., these values obtained being 50.013 c.c., 50.011 c.c., 50.011 c.c. In checking up the 5 c.c. portions very good agreement was formed. The maximum error from 5 c.c. was ±0.031. The method

of calibration used, tho slow and tedious, gave very satisfactory results. The second burette, which was used for the thiosulphate solutions and for acid, was calibrated by the eye and found to be very accurate, tho somewhat inferior to the burette used for iodine.

Other Apparatus.

The other pieces of apparatus used in this work, flasks, pipettes, etc., were carefully calibrated. The alkyl halide was measured out by means of a special form of pipette designed to prevent the evaporation of easily volatile substances. This pipette is described by Robertson.[1] The constant temperature bath was regulated very carefully at 25°. The construction and use of this bath are described by Robertson.[1]

Preparation of 1-Phenyl-3-thiourazole.

The 1-phenyl-3-thiourazole used in this work was prepared by the method of Acree.[2] 1-Phenyl-3-thiosemicarbazide was made by heating phenylhydrazine, ammonium thiocyanate and dry hydrochloric acid in absolute alcohol several hours. The crude product was filtered off, washed with a little alcohol and then lixivated thoroughly with water to remove completely the ammonium chloride and other salts. It was then recrystallized

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[1] Dissertation, Baltimore, 1910.

[2] Ber. d.d. Chem. Ges., 36, 3151.

from alcohol, when it melted at 198° with decomposition. The 1-phenyl-3-thio semicarbazide was crystallized once ffom alcohol, finely pulverized and sifted, and boiled in acetone with slightly more than one molecular equivalent of chlor ethyl carbonate. The 1-carbethoxy-1-phenyl-3-thiosemicarbazide so formed soon precipitated from the acetone; when once crystallized from alcohol it melted with decomposition at 221.5°. This ester was saponified when warmed carefully with potassium hydroxide, and converted into the corresponding 1-potassium-carboxylate 1-phenyl-3-thiosemicarbazide. 1-Phenyl-3-thiourazole was obtained from this by treatment with hydrochloric acid, the 1-carboxylic acid 1-phenyl-3-thiosemicarbazide splitting out spontaneously a molecule of water and forming the thiourazole ring. The crude 1-phenyl-3-thiourazole was washed, dissolved in dilute potassium hydroxide in the cold and reprecipitated by hydrochloric or sulphuric acid, filtered off, washed carefully with water, then dried first on a clay plate and then in vacuo over H_2SO_4. It melted at 190°. By this method the thiourazole was not obtained pure, It was contaminated probably with the disulphide which it readily forms. When first precipitated the thiourazole is white, but it quickly acquires a yellow tint. Recrystallization from all the common solvents does not seem to effect any purification. In alcohol solution the disulphide is formed quite rapidly. Each sample of thiourazole made was anallyzed and the percentage of pure thiourazole determined.

In making up solutions the weight of this urazole corresponding to the required amount of pure substance was used. The thiourazole prepared in the course of this investigation varied in purity from 94.1 per cent to 98.5 per cent.

Method of Analysis.

To determine the purity of any sample of the 1-phenyl-3-thiourazole about 200 mgs. of the dry substance was weighed out, dissolved in alcohol and titrated with sodium hydroxide by using phenolphthalein as indicator. Two hundred c.c. of water and about 5 c.c. of a 1 per cent filtered starch solution were now added. The solution was titrated with a standard solution of iodine in potassium iodide until a distinct blue color, permanent for several seconds, was obtained. The color fades quite rapidly and a little practice is necessary to obtain consistent results. But with some practice the method is very satisfactory. Much more starch is required than in the ordinary thiosulphate-iodine or other clear solutions, as the precipitate of disulphide obscures the color somewhat. Calculations were made on the basis of the following reactions:-

$$2C_8H_6N_3OSNa + I_2 = C_{16}H_{12}N_6O_2S_2 + 2NaI.$$

In other words one atom of iodine is equivalent to one molecule of 1-phenyl-3-thiourazole. The iodine solution was titrated against sodium thiosulphate solution which had been standardized against weighed portions of pure iodine. The iodine used for standardizations was sublimed once from potassium iodide and then resublimed.

In making up solutions chemically pure resublimed iodine was used.

Preparation of Absolute Alcohol.

The absolute ethyl alcohol used in making up thiourazole and alkyl halide solutions was prepared by boiling ordinary 95 per cent alcohol with lime 2-6 days, distilling, boiling the distillate with fresh lime several days longer and distilling the alcohol into a bottle carefully protected from the moisture of the air throughout the process. During the treatment with lime the alcohol often boiled up through the condenser unless the apparatus was carefully watched. This difficulty was overcome by running a small lead pipe through two holes in the stopper in such a way that a small coil was formed just below the stopper and inside the flask. When water was run through this lead coil it proved a very effective condensing agent and scarcely any alcohol was seen dropping from the bottom of the condenser even during rapid boiling.

Ethyl Iodide.

Crude ethyl iodide was distilled from phosphorus pentoxide and very carefully fractionated by using a calibrated thermometer of great accuracy.
A fraction was obtained boiling 72.42° -72.44° at 760mms. and this was used in the work.

Preparation of Solutions.

In making up a solution of ethyl iodide 0.1 per cent excess was used in all cases. The required amount was calculated and the corresponding volume intro-

duced was ascertained by weighing. The flask was placed in the 25° bath and allowed to come to constant temperature and alcohol was added to give the required volume corresponding to the weight of the ethyl iodide. To make the urazole salt a solution of sodium ethylate was prepared by dissolving metallic sodium in cold absolute alcohol. This was made up in such a strength that when 25 c.c. or 50 c.c. were placed in a 100 c.c. flask, only a few c.c. of alcohol had to be added above the mark to secure the desired normality. The exact concentration was determined by titration with N/5 HCl and methyl orange. The weight of 1-phenyl-3-thiourazole corresponding to the required normality in this volume was calculated. This quantity was divided by the per cent of putity of the sample of urazole at hand, and this quantity, plus 0.5 mg. allowed for loss in transferring, was weighed out and added to a 100 c.c. flask by means of glazed paper and a camel's hair brush. Then 25 c.c. or 50 c.c., as the case might be, of the ethylate solution were introduced and alcohol was added nearly to the mark. After the solutions had come to 25° alcohol was added to make the required volume. As mentioned above urazole solutions were made up on the basis of the pure substance. It was thought that the imputity present, probably largely the corresponding disulphide, would not interfere with the reaction, and such was found to be the case, as good agreement was found in the constants obtained when urazole of a different purity was used in the preparation of the solutions.

Procedure in Running a Series.

After the solutions had been made up to the required concentration 10 c.c. portions of the urazole solution were introduced by means of a pipette into small flasks, which were closed with corks and placed in the 25° bath. At the same time two 10 c.c. portions were pipetted into beakers, treated with 200 c.c. of water and about 5 c.c. of starch solution, and titrated with the standard iodine solutions. The mean of the two titrations were taken as the value A, the initial concentration of the urazole. In other words the concentrations of the reacting substances are expressed in cubic centimeters of iodine solutions. For the higher concentrations a N/10 iodine solution was used and for the most dilute N/20 and N/30 solutions were used. When the temperature of the urazole solution in the flasks had reached 25°, 10 c.c. portions of the ethyl iodide solutions were introduced by means of the special pipette. The time when half of the solution had been introduced was taken as the beginning of the reaction. Each tube was filled by this method, shaken several times and replaced in the bath as quickly as possible, the time being noted. After suitable intervals after the time of filling, the tubes were removed from the bath and poured into 200 c.c. of water, the solutions adhering to the tube and cork being carefully washed into the beaker. Starch was added and

the solution titrated with the iodine solution used to determine A. The number of c.c. required is A-x. It was possible to determine the end point very accurately if sufficient starch was used. Generally six tubes were used for each run and the time periods were 10, 20, 30, 45, 60, 75 minutes. The solutions used in this work had the following concentrations after mixture:

Sodium 1-phenyl-3-thiourazole :-	$\frac{N}{4}$	$\frac{N}{8}$	$\frac{N}{16}$	$\frac{N}{32}$	$\frac{N}{32}$	$\frac{N}{64}$
	+	+	+	+	+	+
Ethyl iodide:-	$\frac{N}{4}$	$\frac{N}{8}$	$\frac{N}{16}$	$\frac{N}{8}$	$\frac{N}{32}$	$\frac{N}{8}$

In the N/32 and N/64 solutions N/4 ethyl iodide was used to increase the speed of the reactions and to secure greater accuracy. In such cases the large excess of ethyl iodide interfered with the indicator, the end point being shown, not by a blue color but by a slight pink color.

In the lower concentrations clear solutions were obtained when the urazole was dissolved by the sodium ethylate but in the N/2 and N/4 solutions a fine yellow insoluble substance, probably the disulphide, was noticed. This did not seem to interfere, however, with the course of the reaction.

Calculations.

When equal molecular quantities are used the equation for the velocity constant is

$$KV = AK = \frac{1}{T} \frac{x}{A-x} \quad \text{when}$$

T is the time of the reaction,

x is the amount of urazole salt changed in the time T,

and A-x is the amount at the end of the time T.

When the amounts of urazole and alkyl halide are not equimolecular the following equations must be used:

$$K_V = \frac{A}{(B-A)\ 0.4343} \quad \frac{1}{T} \log \frac{A(B-x)}{B(A-x)} \quad \text{when}$$

A is the initial concentration of the urazole salt, B is the initial concentration of the alkyl halide, A-x is the concentration of the urazole salt at the time T, B-x is the concentration of the alkyl halide at the time T, T is the duration of the reaction, and 0.4343 is the constant used to change Briggsian logarithms to natural logarithms.

The values of K_V are multiplied by V, the volume containing a gram molecule of the sodium urazole, and the values of K_n corresponding to different values of $\mathcal{L}$ are thus obtained as illustrated in Table XI. When the numbers representing K_n, $\mathcal{L}$, and $(1-\mathcal{L})$ are inserted in the equations:-

$$K_{n1} = K_i \mathcal{L}_1 + K_m (1-\mathcal{L}_1),$$

$$K_{n2} = K_i \mathcal{L}_2 + K_m (1-\mathcal{L}_2), \text{ etc.,}$$

and these equations are solved simultaneously for K_i and K_m we secure the very good constants given in Table XIII. This gives us, then, excellent evidence that both the urazole anions and the non-ionized sodium urazole salt are concerned in the reaction.

When the average values of K_i and K_m, and the different values of $\mathcal{L}_1$, $\mathcal{L}_2$, etc. are substituted in the preceding equations we obtained "calculated" values of K_n which are compared in Table XIV with the "found" values of K_n. These are seen to agree very closely, the experimental error averaging less than 1 per cent.

Table I.

0.25N Sodium 1-Phenyl-3-thiourazole and
0.25N Ethyl Iodide at 25°.

A = 52.86

T	A-x	x	K_V
10	33.79	19.07	0.0564
20	24.49	28.37	0.0579
45	15.09	37.37	0.0556
60	12.09	40.77	0.0562
75	10.20	42.66	0.0558

Average K_V = 0.0564

K_n = 0.226

Table II.

0.25 N Sodium 1-Phenyl-3-thiourazole.
0.25 N Ethyl Iodide at 25°.

A = 52.51

T	A-x	x	K_V
10	33.53	18.98	0.0566
20	24.51	28.00	0.0571
30	19.24	33.27	0.0576
50	13.73	38.78	0.0565
60	12.02	40.49	0.0561

Average K_V = 0.0563

K_n = 0.227

Table III.

0.125 N Sodum 1-Phenyl-3-thiourazole and

0.125 N Ethyl Iodide at 25°.

$A = 26.30$

T	A-x	X	K_V
10	19.98	6.32	0.03163
20	16.02	10.28	0.03208
30	13.37	12.93	0.03224
45	10.76	15.54	0.03209
60	9.00	17.30	0.03204
90	6.76	19.54	0.03212

Average K_V = 0.03203

K_n = 0.256

Table IV.

0.125 N Sodium 1-Phenyl-3-thiourazole and

0.125 N Ethyl Iodide. at 25°.

$A = 26.50$

T	A-x	x	K_V
10	19.98	6.52	0.03263
19.33	16.10	10.40	0.03257
30	13.40	13.10	0.03259
40	11.55	14.95	0.03236
50	10.21	16.29	0.03191
60	9.09	17.41	0.03192

Average K_V = 0.03233

K_n = 0.259

Table V.

0.0625 N Sodium 1-Phenyl-3-thiourazole and

0.0625 N Ethyl Iodide at 25°.

$A = 13.26$

T	A-x	x	K_V
10	11.19	2.07	0.01850
20	9.71	3.55	0.01823
30	8.58	4.68	0.01818
45	7.36	5.90	0.01781
60	6.40	6.86	0.01774
75	5.69	7.57	0.01778
90	5.10	8.16	

Average K_V = 0.01802

K_n = 0.288

Table VI.

0.0625 N Sodium 1-Phenyl-3-thiourazole and

0.0625 N Ethyl Iodide at 25°.

$A = 13.26$

T	A-x	x	K_V
10	11.24	2.02	0.01797
20	9.72	3.54	0.01821
30	8.58	4.68	0.01818
45	7.29	5.97	0.01820
60	6.35	6.91	0.01814
75	5.61	7.65	0.01818

Average K_V = 0.01815

K_n = 0.290

Table VII.

0.03125 N Sodium 1-Phenyl-3-thiourazole and

0.03125 N Ethyl Iodide at 25°.

T

A = 6.64

T	A-x	x	K_v
10	6.04	0.60	0.00993
20	5.56	1.08	0.00971
30	5.11	1.53	0.00998
45	4.60	2.04	0.00986
60	4.19	2.45	0.00975
75	3.89	2.75	0.00943
90	3.60	3.04	0.00938

Average K_v = 0.00972

K_n = 0.311

Table VIII.

0.03125 N Sodium 1-Phenyl-3-thiourazole and

0.125 N Ethyl Iodide at 25°.

A = 20.16 B = 80.64

T	A-x	B-x	x	K_v
10	13.81	74.24	6.35	0.00988
20	9.76	70.24	10.40	0.00979
30	6.91	66.39	13.25	0.00974
40	5.01	64.49	15.15	0.00974
50	3.55	63.03	16.61	0.00994
60	2.72	62.20	17.44	0.00968

Average K_v=0.00980

K_n=0.314

Table IX.

0.015625 N Sodium 1-Phenyl-3-thiourazole and

0.125 N Ethyl Iodide at 25°.

A = 9.81 B = 78.48

T	A-x	B-x	x	K_V
10	6.49	75.16	3.32	0.00528
20	4.37	73.04	5.44	0.00526
30	2.93	71.60	6.88	0.00532
40	2.00	70.67	7.81	0.00531
50	1.43	70.10	8.38	0.00518
60	1.03	69.70	8.78	0.00508

Average K_V = 0.00524

K_n = 0.335

Table X.

0.015625 N Sodium 1-Phenyl-3-thiourazole and

0.125 N. Ethyl Iodide at 25°.

A = 14.42 B = 115.36

T	A-x	B-x	x	K_V
10	9.54	110.48	4.88	0.00528
20	6.40	107.34	8.02	0.00529
30	4.32	105.26	10.10	0.00530
45	2.50	103.44	11.92	0.00522
60	1.47	102.41	12.95	0.00515
75	0.90	101.34	13.52	(0.00611)

Average K_V = 0.00525

K_n = 0.336

Table XI.

K_V and K_N for Sodium 1-Phenyl-3-thiourazole and Ethyl Iodide at 25°.

V	K_V		K_N mean
4	0.0564	0.0566	0.2265
4	0.0568		
8	0.03203	0.03218	0.2575
8	0.03233		
16	0.01802	0.01809	0.289
16	0.01815		
32	0.00972	0.00976	0.3125
32	0.00980		
64	0.00524	0.005245	0.3355
64	0.00525		

Table XII.

Ionization of Sodium 1-Phenyl-3-thiourazole at 25°.

V	$\mathcal{L}$	(1-$\mathcal{L}$)
4	29.8	70.2
8	39.0	61.0
16	49.5	50.5
32	56.6	43.4
64	[illegible]	[illegible]

Table XIII.

K_i and K_m for Sodium 1-Phenyl-3-thiourazole and Ethyl Iodide at 25°.

	K_i	K_m
V = 4 : V = 8	0.452	0.131
V = 4 : V = 16	0.450	0.132
V = 4 : V = 32	0.455	0.131
V = 8 : V = 16	0.446	0.135
V = 8 : V = 32	0.427	0.131
V = 16: V = 32	0.450	0.125
Mean	0.447	0.131

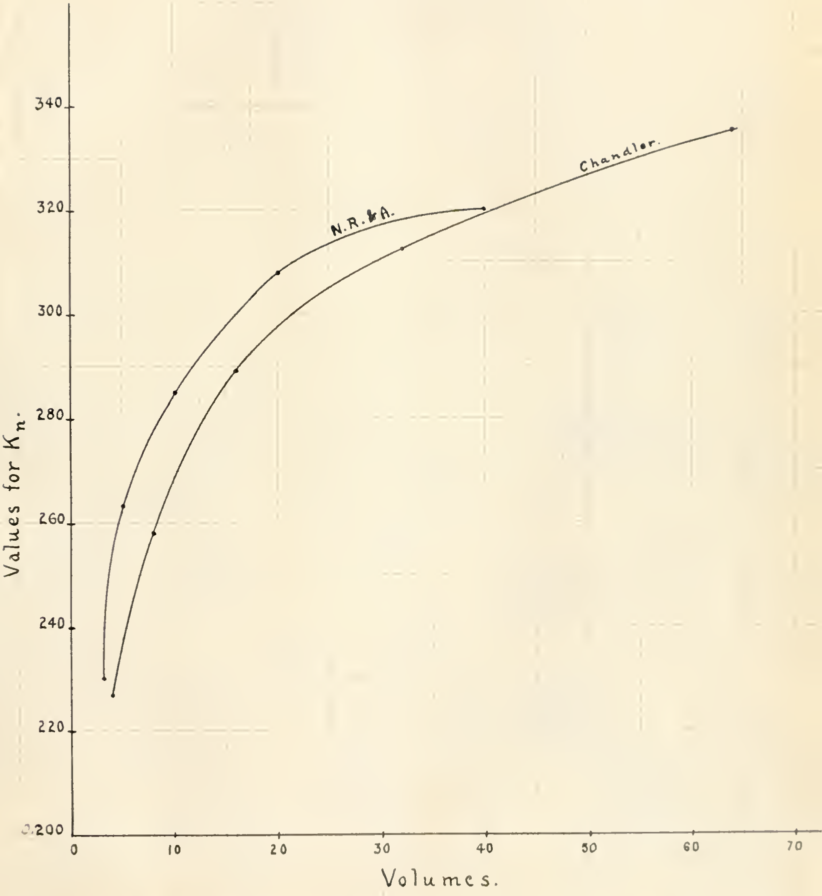
$K_i : K_m = 3.43$

Table XIV.

"K_n found" and "K_n calculated" for Sodium 1-Phenyl-3-thiourazole and Ethyl Iodide at 25°.

V	K_n calculated	K_n found
4	0.2253	0.2265
8	0.2583	0.2575
16	0.2875	0.2890
32	0.3099	0.3125
64		

On the next page is given a set of curves showing the values of K_n at the different concentrations studied by Nirdlinger andRogers, and the values of K_n obtained by Chandler. It is seen that these two curves are not identical, although they are very close together. This is accounted for by the fact that the solutions worked with by Nirdlinger and Rogers contained water which varied in amount from 0.15 per cent to 1.2 per cent. A correction will be made forthis later.


Values for K_n.
340
320
300
280
260
240
220
0.200
0
10
20
30
40
50
60
70
Volumes.
N.R.&A.
Chandler.

In the following tables are presented the results obtained when sodium iodide is added to N/64 and N/32 sodium 1-phenyl-3-thiourazole and ethyl iodide. The ~~t~~ alteration ~~tension~~ of the reaction velocity is very close to that calculated on the assumption that the decrease is due chiefly to the change in the ionization of the sodium urazole produced by the added sodium iodide. This change in ionization has been calculated on the basis of the Arrhenius' theory of isohydric solutions.

Table XV.

0.015625 N Sodium 1-Phenyl-3-thiourazole, 0.125 N Ethyl Iodide and 0.015625 N Sodium Iodide at 25°.

A = 7.58 B = 60.64

T	A-x	x	B-x	K_V
10	5.17	2.41	58.23	0.004987
20	3.56	4.02	56.62	0.004907
30	2.50	5.08	57.56	0.005034
40	1.73	5.88	58.76	0.005062
50	1.29	6.29	59.35	0.004993
60	0.93	6.65	59.71	0.004959

Average K_V = 0.4975

K_n = 0.313

Table XVI.

0.015625 N Sodium 1-Phenyl-3-thiourazole, 0.125 N Ethyl Iodide and 0.015625 N Sodium Iodide at 25°.

A = 7.50 B = 60.00

T	A-x	x	B-x	K_V
10	5.17	2.33	57.67	0.00475
20	3.56	3.94	56.06	0.00434
30	2.50	5.00	55.00	0.00482
40	1.73	5.72	54.23	0.00478
50	1.29	5.21	54.79	0.00477
60	0.93	6.57	53.43	0.00469

Average K_V = 0.00478

K_n = 0.306

Table XVII.

0.015625 N Sodium 1-Phenyl-3-thiourazole, 0.125 N Ethyl Iodide and 0.015625 N Sodium Iodide at 25°.

A = 7.50 B = 60.00

T	A-x	x	B-x	K_V
10	5.10	2.40	57.60	0.004927
20	3.50	4.00	56.00	0.004951
30	2.47	5.03	54.97	0.004875
40	1.73	5.77	54.23	0.004877
50	1.27	6.23	53.77	0.004763

Average K_V=0.00488

K_n=0.312

Table XVIII.

015625

0.03125 N Sodium 1-Phenyl-3-yhiourazole, 0.125 N Ethyl Iodide and

46875

0.09375 N Sodium Iodide.

A = 7.46 B = 59.66

T	A-x	x	B-x	K_V
10	5.24	2.22	57.46	0.004505
20	3.70	3.76	55.92	0.004542
30	2.71	4.75	54.93	0.004427
40	2.01	5.45	54.23	0.004342
50	1.46	6.00	53.68	0.004353
60	1.10	6.36	53.32	0.004290

Average K_V = 0.004411

K_n = 0.282

$\log K_n$ = [illegible]

Table XIX.

0.03125 N Sodium 1-Phenyl-3-thiourazole, 0.125 N Ethyl Iodide and 0.09375 N Sodium Iodide.

A = 7.46 B = 59.68

T	A-x	x	B-x	K_V
10	5.20	2.26	57.42	0.00453
20	3.75	3.71	55.97	0.00445
30	2.70	4.76	54.92	0.00444
40	1.97	5.49	54.19	0.00441
50	1.45	6.01	53.67	0.00438
60	1.07	6.39	53.29	0.00435
70	0.31	6.55	53.03	0.00429

Average K_V = 0.00441

K_n = 0.282

Table XX.

0.03125 N Sodium 1-Phenyl-3-thiourazole, 0.125 N Ethyl Iodide and 0.03125 N Sodium Iodide at 25°.

A = 15.09 B = 60.36

T	A-x	x	B-x	K_V
10	10.77	4,32	56.04	0.00377
20	7.88	7.21	53.15	(0.00374)
30	5.70	9.30	50.97	0.00394
40	4.27	10.32	49.54	0.00387
50	3.17	11.92	48.44	0.00394
60	2.40	12.69	47.67	0.00390
70	1.83	13.26	47.10	0.00384

Average K_V = 0.00385

K_n = 0.283

Table XXI.

0.03125 N Sodium 1-Phenyl-3-thiourazole, 0.125 N Ethyl Iodide and 0.03125 N Sodium Iodide at 25°.

A = 15.04 B = 60.16

T	A-x	x	B-x	K_v
10	10.71	4.33	55.83	0.00883
20	7.73	7.31	52.85	0.00893
30	5.75	9.29	50.87	0.00882
40	4.26	10.78	49.38	0.00887
50	3.19	11.85	48.31	0.00883
60	2.44	12.60	47.50	0.00879
			Average K_v	= 0.00885
			K_n	= 0.283

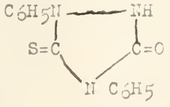
Reactions Involving Both Ions and Molecules.

Substances	Temperature	K_i	K_m	$K_i : K_m$
C_6H_5ONa and CH_3I	25°	0.0282	0.00474	5.95
C_6H_5ONa and CH_3I	35°	0.091	0.0135	6.74
C_2H_5ONa and CH_3I	25°	0.127	0.0594	2.13
C_2H_5ONa and C_2H_5I	25°	0.0120	0.00427	2.81
C_2H_5ONa and C_2H_5Br	25°	0.005760	0.00233	2.41
C_2H_5ONa and C_6H_5CN	25°	0.1148	0.1003	1.14
C_2H_5ONa and CH_3CN	25°	0.344	0.228	1.51
$C_3H_6N_3OSNa$ and C_2H_5I (Nirdlinger and Rogers)	25°	0.43	0.17	2.5
$C_3H_6N_3OSNa$ and C_2H_5I (Chandler)	25°	0.447	0.131	3.4

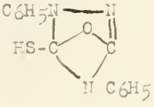
II. A STUDY OF 1,4-DIPHENYL-5-THIOURAZOLE.

1, 4-Diphenyl-5-thiourazole was first prepared by Marckwald[1] from 2,4-diphenyl-3-thiosemicarbazide and phosgene. It was suppoeed by him to be a 3-thio compound. That the sulphur is really in position 5, was established by the work of Busch and Holzmann[2] and Nirdlinger and Acree[3]. Busch and his co-workers found that when 2,4-diphenyl-3-thiosemicarbazide was treated in the cold with phosgene a substance was obtained which melted at 139°, but which, when heated just below the melting point or when recrystallizated from alcohol, very readily rearranged into an isomeric compound which melted at 219°-222°. This latter substance was found to be identical with the compound obtained by Marckwald.

Busch and his co-workers thought at first that the lower melting isomer is 1,4-diphenyl-5-thiolurazole, Formula (II), and the higher melting isomer, 1,4-diphenyl-5-thiourazole, Formula (I).



I.



II.

These two isomeric diphenyl-thiourazoles seemed to offer a good example of tautomerism and a study of these compounds from this point of view was undertaken by

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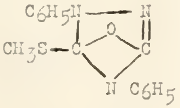
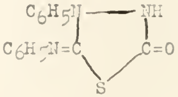
[1] Ber.d.Deut.Chem.Ges., 25, 3093.
[2] Ber. d.Deut.Chem. Ges., 34,320.
[3] Nirdlinger's Dissertation, Baltimore, 1909, p 34.

Nirdlinger and Acree[1]. They accepted at first the formulas of Busch. Their results, however, soon led them to the conclusion that the high melting isomer is certainly a thiol acid, Formula (II), and the low melting isomer probably the thion acid, formula (I). Busch later came to the same conclusion.

The problem was then taken up by Dr. E.P.Doetsch[2]. He studied the velocity of the rearrangement of the sodium salt of the thion acid into the thiol form at 20°. From his results he was led to believe, as Nirdlinger and Acree had assumed, that the rearrangement of thion into a thiol salt is a reversible reaction. One experiment carried out by him is of special interest. He saponified the methyl ester of 1,4-diphenyl-5-thiolurazole, formula (III), with potassium sulphhydrate and obtained a compound that first melted at 141°, then solidified, and then melted at 220 °, and which he therefore supposed to be the thion acid, formula (I).



III.



IV.

In 1911 Busch and Limpacht[3] published an article in which they attacked the work of Nirdlinger and Acree. They claimed that the substance formed when

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[1] Nirdlinger, Dissertation, Baltimore, 1909, p 34.

[2] Doetsch, Dissertation, Baltimofe, 1911.

[3] Ber.d.Deut.Chem. Ges. 44, 560.

2,4-diphenyl-3-thiosemicarbazide reacts with phosgene is not diphenyl-thiourazole, formula (I), but phenyl-anilido thiobiazolone, formula (IV). This, when heated, rearranges into diphenyl-thiolurazole, but, according to Busch and Limpacht, the reverse rearrangement of the thiolurazole into a thiobiazolon does not take place.

The main problem in the present investigation was the preparation of 1,4-diphenyl-5-thiolurazole in the pure state by a new method. Nirdlinger and Doetsch had never obtained this compound pure, as it had always been mixed with the lower melting isomer. The experiment of Doetsch in which he saponified the methyl thiolester of 1,4-diphenyl-5-thiolurazole with potassium sulphhydrate was repeated at 0°. A compound was obtained which showed no signs of melting at 141°, and which melted at 218°-219°. After recrystallization from alcohol it melted at 220.5-221.5. This experiment was repeated several times and in no case was a compound melting at 141° obtained. When saponification was carried out in absolute alcoholic solution the result was the same. Apparently the product obtained by this reaction is quite pure 1,4-diphenyl-5-thiolurazole. The purity, however, has not been determined by analysis. From the method of preparation no thiobiazolon would be expected to be present. It may be an equilibrium misture of a large proportion of 1,4-diphenyl-thiolurazole, formula (II), and a small proportion of 1,4-diphenyl-5-thiourazole, formula (I). This question and that of the structure of the low melting product obtained from 2,4-diphenyl-3-thiosemicarbazide and phosgene will be investigated.

EXPERIMENTAL.

Thiocarbanilide.

The ordinary method[1] for the preparation of this compound by heating aniline and carbon disulphide in alcoholic solution with potassium hydroxide did not give very good yields. The improvement discovered by Hugershoff[2] and described by Gattermann[1] was then tried and found to be entirely satisfactory. The method consists in heating equal parts (100 grams) of aniline, carbon disulphide and alcohol with a small quantity (1 gram) of sulphur five or six hours. When the reaction was complete, the excess of alcohol and carbon disulphide was evaporated. Water was added to the residue and the crude thiocarbanilide was filtered off, washed with water, and dried in the air. The yield was practically quantitative. It was found impracticable to dry the thiocarbanilide in an air bath for decomposition took place even at 110°. The air dried product was used without further purification for the preparation of phenyl mustard oil.

Phenyl Mustard Oil.

The most satisfactory method for obtaining phenyl mustard oil from thiocarbanilide was found to be the following:- 100 grams of water was placed in a 1 liter balloon flask with a long neck and mixed with

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[1] Gattermann: Die Praxis des Organischen Chemikers, 9th edition, p. 203.

[2] Ber. d Deut. Chem. Ges., 32, 2245.

100 grams of concentrated sulphuric acid. To the hot acid was added 100 grams of thiocarbanilide and the flask was then arranged for steam distillation. The flask containing the thiocarbanilide was heated to boiling and steam led in. The reaction took place in a very few moments and the mustard oil distilled over in half an hour. The crude mustard oil was separated from the water, washed with water, dried with calcium chloride, and redistilled. A product was obtained which boiled at 217°-218°. About 40 grams of crude phenyl mustard oil were ordinarily obtained from 100 grams of air-dried thiocarbanilide.

2,4-Diphenyl-3-thiosemicarbazide.

This compound was prepared by the method of Marckwald,[1] which gave quantitative yields. A cold alcoholic solution of phenyl hydrazine was treated with a cold alcoholic solution of phenyl mustard oil; the resulting product was filtered off, washed with a little cold alcohol, and dried in the air. The crude product had a very slight pink color, and melted at once when plunged into a sulphuric bath heated to 137°. Owing to a rearrangement into 1,4-diphenyl-3-thiosemicarbazide the melting point cannot be determined in the usual way. Recrystallization from hot benzene did not seem to effect any further purification.

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[1] Ber.d.Deut. Chem. Ges., 25,3106.

See Nirdlinger, Dissertation, Baltimore,1909, page 50.

2,4-Diphenyl-3-methylthiolsemicarbazide.

The method described by Busch and Holzmann[1] was used for the preparation of the compound. The crude diphenyl thiosemicarbazide was finely ground and passed through a No. 60 sieve. A weighed amount of the finely divided product was treated with the theoretical quantity of a 10 per cent solution of alcoholic potassium hydroxide and a slight excess of methyl iodide, and heated gradually with constant shaking until a clear solution was obtained. The reaction mixture was then cooled in ice and salt. The precipitate obtained at once was largely potassium iodide. After long standing in ice and salt the desired ester crystallized out. The crude ester was filtered off, washed with a little very cold alcohol, then with water to remove the potassium iodide, and then recrystallized from alcohol. The purified ester had only a very faint pink color and melted at 75.5°-76°. Fifty grams of 1,4-diphenyl-3-thiosemicarbazide gave 32 grams of the methyl ester. The addition of the methyl iodide before heating is absolutely essential, as very little of the desired ester is otherwise obtained, the main product being a dark brown tarry mass with a very bad odor.

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[1] Ber. d. Deut.Chem. Ges., 34, 335.

1,4-Diphenyl-5-methyl thiolurazole.

This compound was made by the method of Busch and Holzmann,[1] slightly modified. A solution of 2,4-diphenyl-3-methyl-thiolsemicarbazide in benzene was added to a 20 per cent solution of phosgene in dry toluene. The reaction was carried out at 0° and the solutions were protected from the moisture of the air by calcium chloride tubes. The precipitate was freed as much as possible from the solution, washed with water, dried in the air, and precipitated from absolute alcoholic solution with ether. The reprecipitated ester melted, when dried in vacuo over sulphuric acid, at 196°. It was pure white in color. Ten grams of diphenyl-methyl-thiolsemicarbazide gave 7.5 grams of 1,4-diphenyl-5-methyl-thiolurazole.

1,4-Diphenyl-5 thiolurazole.

The thiol acid was prepared by saponification of the methyl-thiol ester with potassium or sodium sulphhydrate at 0°. A weighed quantity of the pure methyl thiolester of 1,4 -diphenyl-5-thiolurazole was dissolved in alcohol. Five per cent more than the molecular quantity of standard alkali was measured into a small flask and saturated with hydrogen sulphide at 0°, and to this was added the alcoholic solution of the thiolurazole ester. The reaction mixture was placed in ice in a Dewar bulb

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[1] Ber. d.Deut.Chem. Ges., 34,340.

and allowed to stand over night. A strong odor of methyl mercaptan was noticeable the next morning. The reaction mixture was treated with water and extracted with chloroform to remove any unchanged ester. The extracted solution was freed from drops of chloroform by filtration, cooled in ice and acidified with acetic acid. If only a very slight excess of acetic acid was used no precipitate was obtained. A large excess, however, produced a white floculent precipitate which showed no softening at 141° and which melted at 220°. When the filtrate, or the clear solution yielding no precipitate when acidified with acetic acid, was treated with hydrochloric acid a dense white precipitate was formed. This was filtered off, washed with water and dried. It showed no softening at 141° and melted at 220°. When recrystallized from alcohol and dried in vacuo over sulphuric acid it melted sharply at 220.5°-221.5°. The compound obtained was undoubtedly 1,4 diphenyl-5-thiolurazole in quite pure state. It could hardly contain any quantity of the isomeric thion acid, or of 1,4 diphenyl urazole, for both of these compounds are doubtless weaker acids than the thiolurazole and hence precipitated from solutions of their alkali salts by a very slight excess of acetic acid. The saponification was also carried out in absolute alcoholic solutions with the same results. In this case the sodium sulphhydrate was prepared by saturating a solution of sodium ethylate in absolute alcohol with hydrogen sulphide.

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    On the Rearrangement of the Tautomeric Salts of 1,4-Diphenyl-5-Thionurazole and 1,4-Diphenyl-5-Thiolurazole.

BIOGRAPHY.

Joseph Chandler the author of this dissertation, was born in Livermore Falls, Maine, January 16, 1889. His parents were George and Isora S. (Hatch) Chandler. His early education was obtained in the public schools of the town of East Livermore. In 1905 he was graduated from the Livermore Falls High School. In September of the same year he entered Colby College, Waterville, Maine, from which institution he received the degree of A.B. in 1909. In October, 1909, he entered the Johns Hopkins University as a post graduate student in Chemistry with Physical Chemistry and Mineralogy as subordinate subjects. During the year 1911-12 he held a University scholarship.